

## IN THE SPECIFICATION

Please replace the paragraph that appears on page 42, lines 2 to 6, with the following paragraph:

In addition to dCTP daminase, *P. furiousus* P45 exhibits a significant, but lower degree of sequence similarity to uridine triphosphatase (dUTPase). dUTPase, an enzyme encoded by the *dut* gene, converts dUTP to pyrophosphate and dUMP. An amino acid sequence alignment comparing the sequence of P45 to several dUTPases is shown below. Regions of identity and regions of similarity are shown in black boxes, while ~~regions of similarity are shown in grey boxes.~~

Please replace the sequence listing that appears after the abstract at page 76 with the enclosed sequence listing.

Please replace page 41 with the replacement page 41 enclosed herewith.

Please replace page 43 with the replacement page 43 enclosed herewith.



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### Example 9

#### Identification of Proteins Related to P45

##### 1. DNA Sequence Homology of *P. furiosus* P45 Protein to dCTP Deaminase and dUTPases

When the P45 DNA sequence was compared to multiple databases using the program BlastX, the probable deoxycytidine triphosphate deaminase (dCTP deaminase) gene (*dcd*) of *Desulfurolobus ambivalens* was found to exhibit the highest degree of similarity. The biochemical properties and physiological role of dCTP deaminase has been studied in *E. coli*, where dCTP deaminase is a homotetramer, which catalyzes the formation of dUTP and NH<sub>3</sub> from dCTP. DNA sequences with similarity to the *E. coli* *dcd* gene have been discovered in other bacteria (*Salmonella typhimurium*, *Haemophilus influenzae*) and in archaea (Ouzounis, C., Kyrpides, N., and Sander, C. Nucl. Acids Res. 23:565-570 (1995); Bult, C.J. et al. Science 273:1058-1073 (1996); Beck, C.J., Eisenhardt, A.R. and Neuhard, J., J. Biol. Chem. 250:609-616 (1975); Fleischmann, R.D. et al., Science 269:496-512(1995)). Amino acid sequence comparisons between *P. furiosus* P45 and the dCTP deaminases from *Desulfurolobus ambivalens* ("A") (also known as *Acidianus ambivalens*, *Sulfolobus ambivalens*), *E. coli* ("E"), and *Haemophilus influenza* are shown below, demonstrating sequence similarity ranges from about 39.1 to about 71.2%.

#### MAP Multiple Sequence Alignment Results

##### Page 1.1

	1	15	16	30	31	45	46	60	61	75	76	90		
1 P45	MLLPDW	KIRKE	---	-ILIEPFVSE	-EWLQF	AGYD	LVRVGXX	XRVGR	---	RAXVKGK	---	-LIDV	REYAL	
2 A.	MILCDRDL	KYVL	BEG	WIVISPLTQ	-DTTR	NGV	DLRVG	-EIA	R PKTD	BIYEDCKDPR	SPYBIEK	---	-GDEFI	IYPNEHVL
3 E.	MRLCD	CDIRE	AWLDBG	RLSINPRP	VVERING	ATVDV	RIGNKFR	FTR	GHTAA	FIDLSGP	KDB	VSAALDRVMSD	BIVL	
4 HAEIN	MRLCD	TDLERYL	DDG	IISLT	PRPNNDK	ING	ATIDV	RIGNSP	RVPR	BHSAP	FIDLSGP	KEE	VSAQLESV	VMSDEIII
														PEGEAFFLHPGTLAL

##### Page 2.1

	91	105	106	120	121	135	136	150	151	165	166	180	
1 P45	ILTLERIKL	PPDV	MG	DMKIR	SSLARE	GVIG	SPAW	--VDP	GWDG	NL	TLM	YNASN	EPVELR
2 A.	LVT	EEV	VKL	PND	VMA	PVN	LRSSP	PARL	GLPV	YGERP	VQIA	PIRLEG	PARNPYR
3 E.	ATL	LESV	VTP	PADL	IVG	WLD	GRSSL	ARL	GLMV	TIE	VLG	-SAPPV	KIK
4 HAEIN	ATT	LESV	VKL	PANI	IG	WLD	GRSSL	ARL	GLMV	HVA	HRIDPG	MSG	C1

##### Page 3.1

	181	195	196	210	211	225	226	240	241	255	256	270	
1 P45	GSTR	LA	PSK	RKK	KL	162	SEQ ID NO: 91						
2 A.	GOOG	VTL	LPK	PK	KFR	173	SEQ ID NO: 91						
3 E.	NCQG	A	AVAS	R	IDKD	193	SEQ ID NO: 92						
4 HAEIN	NCQG	A	AVAS	R	IDKD	195	SEQ ID NO: 93						

*E. coli* DCD exhibits an apparent molecular weight of 21.2kD (Wang, L. and Weiss, B. J. Bacteriol. 174:5647-5653 (1992)), while the predicted molecular weight of *M. jannaschii* DCD is approximately 22kD (204 amino acids). These molecular weights are approximately half the apparent molecular weight of *P. furiosus* P45 and suggest that the heat-dissociated form of P45

p45	1	MLIDPDWKRKEELIIEPFSEEWLQP
phager1	1	WTTRGKTKNENTTTFEFAT
ECOLI	1	-EHS
HAEIN	1	-MKKIDKQDPPFGKEPEPPTYAT
Scerevisiae	1	-MCKIDKQDLSPEIGNEFPPTYAT
swine	1	-MTPASDKVUNIQRSASATPTKGS
tomato	1	-MSLYVKCVRLSNNAITIPNPSM
variola	1	-SGS
ORFN2	1	-ATA
Human	1	-MENNININSPRENTENRAGPTROS
Rat	1	-PYA
EIAV	1	-MECHETEQWURSONQTIPRGS
consensus	1	-PGI
		-PARISEHETPTGRS
		-ARA
		-DASIREVRILSEHETPTGRS
		-ARA
		-OIKEKREDD

m i k is a lptras  
a

p45	25	:AGYDILRVGKXXRUGREAXVKKGKLIDVKEGKVXUIPRAYAIIILERIKLEDDWMIDMKI-PSLAREGYI-GSFPAWPGDENITMLYMASNP
phager1	23	:AGYDISHG-
ECOLI	28	:AGDLDRGCG-
HAEIN	28	:AGDLDRALI-
Scerevisiae	29	:AGYDIVMSQ-
swine	25	:AGYDLYSA-
tomato	52	:AGYDLYSSAR-
variola	30	:AGYDLYSAV-
ORFN2	29	:AGYDLYSAV-
Human	46	:AGYDLYSAV-
Rat	85	:AGYDLYSAV-
EIAV	34	:AGFDICVY-
consensus	101	:AGYDLYSAV-

d tippe e iv tail i ip  
ygrma prslavkr id199  
gvid dyrgn 19vlyng e

p45	120	VELRYCPEFFVIAFFI-EL-
phager1	101	VTISKSCIMMGVFVNMTT-----NDNNANGNRGTVGGGSTBV-
ECOLI	108	FNIQPSBIAQMIVFVNQRC-FNLBDFATDRCGGFGHSGCR-Q-
HAEIN	108	FKEVGDRAQOLVVFVNQRC-FNLBDFATDRCGGFGHSGCR-Q-
Scerevisiae	104	FALKGDRAQOLIYRITYPE-LKEVQSLSTDRODQGFGSTGL-R-
swine	100	FNLVGDRAQOLIYRITYPE-LKEVQSLSTDRODQGFGSTGL-R-
tomato	127	FEVHGDRARQLIVKIVVTP-VEQDLDSTVGGGGGSTV-
variola	104	FNVTGDRARQLIYRITYPE-LKEVQSLSTDRODQGFGSTGL-R-
ORFN2	104	FEVHKGDRAQOLICERISCPA-VQENKCLDTDRQSGFGSTS-GACGGRTAWIS
Human	121	FEVHKGDRAQOLICERISCPA-VQENKCLDTDRQSGFGSTS-GACGGRTAWIS
Rat	160	FEVHKGDRAQOLICERISCPA-VQENKCLDTDRQSGFGSTS-GACGGRTAWIS
EIAV	108	IKLIECQHARQQLILO-HHSNSRQPDENKISQGKGFGSTGVFWVENIGAQDEHENWHTSPKILARNYKIPLTVAQQTQECPHCTKQGSGPAGCM
consensus	201	f ik GariaQlit ril pe i v ld targ 99fgstg

SEQ ID NO: 71  
SEQ ID NO: 93  
SEQ ID NO: 94  
SEQ ID NO: 93  
SEQ ID NO: 96  
SEQ ID NO: 97  
SEQ ID NO: 98  
SEQ ID NO: 99  
SEQ ID NO: 100  
SEQ ID NO: 101  
SEQ ID NO: 102  
SEQ ID NO: 103  
SEQ ID NO: 104